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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,489	11/03/2003	Gennady Merkulov	CL001103CON	4936

25748 7590 02/23/2006

CELERA GENOMICS
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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,489	MERKULOV ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 17 to 30 are pending in the instant application. Claims 1 to 16 have been canceled and claims 17 to 30 have been added as requested by Applicant in the correspondence filed 15 August of 2005.

2) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser executable code. For example, see line 2 of page 2 and lines 1 and 2 on page 5. Applicant is required to delete the embedded hyperlink and/or other form of browser executable code. See MPEP § 608.01(p), which states that:

> "When a patent application with embedded hyperlinks and/or other forms of browser executable code issues as a patent (or is published as a patent application publication) and the patent document is placed on the USPTO web page, when the patent document is retrieved and viewed via a web browser, the URL is interpreted as a valid HTML code and it becomes a live web link. When a user clicks on the link with a mouse, the user will be transferred to another web page identified by the URL, if it exists, which could be a commercial web site. USPTO policy does not permit the USPTO to link to any commercial sites since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. If hyperlinks and/or other forms of browser executable code are embedded in the text of the patent application, examiners should object to the specification and indicate to applicants that the embedded hyperlinks and/or other forms of browser executable code are impermissible and require deletion."

Correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3) Claims 17 to 30 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant claims are drawn to an antibody that binds to a protein comprising or

consisting of the amino acid sequence presented in SEQ ID NO:2 of the instant application, and which is identified therein as a human transporter protein. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect or to diagnose or treat by employing antibodies thereto.

It is clear from the instant specification that the transporter protein described therein is what is termed an "orphan transporter" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein, a nucleic acid encoding it and an antibody that binds specifically thereto may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. Whereas one could readily employ a putative transporter protein of the instant invention in an assay to identify potential agonists and antagonists thereto the information obtained thereby would be of little use until one discovers the identity of those physiological processes moderated by that putative transporter. Because the instant specification has failed to credibly identify a physiological process which has been shown to be influenced by the activation or inhibition of a putative transporter protein of the instant invention an artisan would have no way of predicting what effects the administration of an agonist or antagonist thereto to an organism would have. If one can not predict the effects that the administration of an agonist or antagonist of the

putative transporter of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that agonist or antagonist. Further, one could readily employ antibodies to that protein to detect it in a sample or to purify it. However, because the instant specification has failed to attribute any significance to the presence or absence of that protein in a sample, a process of detecting that protein provides no immediate benefit to the public.

The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point where specific benefit exists in currently available form there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to an antibody that specifically binds to a protein of as yet undetermined function or biological significance. Until some actual and specific

significance can be attributed to the putative transporter protein described in the specification, the instant invention is incomplete. To employ a protein of the instant invention in the identification of substances which inhibit or induce its activity, without being able to predict what clinical effects of those compound will have based upon their ability to inhibit or induce that protein to is clearly to employ that protein as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the transporter protein described therein then the claimed antibody is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

The text on pages 36 and 37 of the instant specification essentially teaches that antibodies to a protein of the instant invention can be employed in tissue typing. The employment of a protein of the instant invention, or an antibody that binds to that protein, as a tissue specific marker is not a substantial or specific utility. All human proteins can invariably be classified into two categories, those which are expressed in a tissue or developmentally specific manner and those which are expressed ubiquitously. It can be alleged that an antibody specifically binding to any protein that is expressed in a tissue specific manner can be employed to detect the tissue in which it is expressed in a sample. Alternately, an antibody that specifically binds to a human protein that is expressed ubiquitously can be employed to detect the presence of any human tissue in a sample. Such utilities are analogous to the assertion that a particular protein can be employed as a molecular weight marker, which is neither a specific or substantial utility.

One could just as readily argue that any purified compound having a known structure could be employed as an analytical standard in such processes as nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and mass spectroscopy as well as in polyacrylamide gel electrophoresis (PAGE), high performance liquid chromatography (HPLC) and gas chromatography. None of these processes could be practiced without either calibration standards having known molecular structures or, at least, a range of molecular weight markers having known molecular weights. One could further extrapolate upon this premise by asserting that any item having a fixed measurable parameter can be employed to calibrate any machine or process which measures that parameter. For example, any item having a constant mass within an acceptable range can be employed to calibrate a produce scale in a grocery store. The calibration of produce scales is certainly an important function since most states require produce scales to be calibrated and certified. Therefore, to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object. It was just such applications that the court appeared to be referring to when it expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation (*Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966)). Because the steroid compound which was the subject of that decision had a known structure and molecular weight it could have readily been employed as a molecular standard at that time. Further, because that compound was a

hydrocarbon it certainly could have been employed in the well known process of combustion for purposes of lighting and/ or the generation of heat. The generation of heat by combustion of hydrocarbons certainly was and remains an important process. Irrespective of such obvious utilities, the court still held that the compound produced by the process at issue in *Brenner v. Manson* did not have a specific and substantial utility.

To grant Applicant a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" *(Brenner v. Manson, Ibid)*. To grant Applicant a patent on the claimed antibody based solely upon an assertion that the protein bound thereby can be employed as a tissue marker is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted and would be no different than granting a patent on the process disputed in *Brenner v. Manson* on the premise that the steroid produced thereby was useful as an analytical standard or as a combustible fuel source.

Further, the expression data presented in Figure 1 that suggests that a protein of the instant invention is expressed selectively "in placenta choriocarcinomas, retina, uterus, leiomyosarcomas, breast, ovary fibrotheomas, and leukocytes" does not support a conclusion that the protein itself exhibits such an expression pattern because that data appears to be based upon the detection of mRNA expression levels. Greenbaum

et al. (Genome Biology, 2003, Vol. 4, Issue 9, pages 117.1-117.8) cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (page 117.3, 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic processes involved in protein synthesis and degradation have to be better understood. Therefore, one of ordinary skill in the art would not reasonably conclude that the claimed antibodies can be used to detect "placenta choriocarcinomas, retina, uterus, leiomyosarcomas, breast,

ovary fibrotheomas, and leukocytes" by reviewing the experimental data provided by the instant specification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) Claims 17 to 30 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

5) Claims 18, 20, 22, 24, 26, 28 and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Because of the presence of the term "wherein the amino acid sequence of said polypeptide **comprises** SEQ ID NO:2", these claims encompass an antibody which binds to an epitope that is not contained within SEQ ID NO:2. It is old and well known in the art that the portion of a protein to which an antibody binds usually consists of no more than six to eight amino acid residues. It was also well known in the art long before the instant invention was made to express a recombinant protein as part of a fusion protein "comprising", in addition to the amino acid sequence of a desired protein, an antigenic tail such as a "FLAG epitope", a polyhistidine tail, or a "Protein A" fragment to facilitate the purification of the desired protein. Because of the presence of the term "comprising" in the instant claims, they encompass any antibody which can bind to any epitope which can be

expressed as a portion of a polypeptide comprising the amino acid sequence as set fourth in SEQ ID NO:2 and, therefore they essentially encompass any antibody which can bind to any polypeptide or protein. The instant specification, however, does not provide a written description or the guidance needed to produce an antibody which binds to any epitope other than an epitope which is contained within SEQ ID NO:2 of the instant application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6) Claims 18, 20, 22, 24, 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by the Hopp et al. patent (5,011,912). As explained above, these claims encompass an antibody which binds to any antigenic peptide, including the flag epitope DYKDDDDK which was bound by the antibody of Hopp et al. prior to the time of the instant invention.

7) Claims 17, 18, 21, 22, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by the Weber et al. publication (P.N.A.S. 94:8509-8514, Aug. 1997). The amino acid sequence of the solute carrier protein of Weber et al. is greater than 95% identical to the amino acid sequence presented in SEQ ID NO:2 of the instant application. The section entitled "**Immuno-Electron Microscopy**" on page 8510 of

Weber et al. described labeled polyclonal antibodies that are most certainly encompassed by the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8) Claims 17 to 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of the Hopp et al. or Weber et al. publications cited above, each in view of the Maurer et al. publication. In so far as these claims encompass a monoclonal antibody, the Maurer et al. review article shows that the production of polyclonal and monoclonal antibodies to a known peptide like those of Hopp et al. and Weber et al. was a practice that was old and well known in the art long before the making of the instant invention, as was the proteolytic fragmentation of such antibodies to yield monovalent reagents for the detection of that peptide in a sample.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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